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Confirmation of the Catania Brachydactylous Type of Acrofacial Dysostosis: Report of a Second Family

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The acrofacial dysostoses (AFD) are a heterogeneous group of disorders combining varying severities of mandibulofacial dysostosis (MFD) with pre- and/or postaxial limb abnormalities. In 1993, Opitz et al. [Am J Med Genet 47:660–678] described a new AFD with mental retardation in a Sicilian mother and her four sons characterized by intrauterine growth retardation (IUGR), postnatal short stature, microcephaly, widow's peak, MFD without cleft palate, mild pre- and postaxial limb hypoplasia with brachydactyly, mild interdigital webbing, and cryptorchidism and hypospadias in males. We report a mother and daughter with this same phenotype, confirming this new type of AFD and expanding the clinical phenotype to include frequent dental caries. Analysis of cephalometric and metacarpophalangeal profiles in this family showed no distinctive diagnostic abnormalities. This family confirms the Catania brachydactylous type of AFD and supports an autosomal dominant mode of inheritance, although male-to-male transmission has not been demonstrated. © 1996 Wiley-Liss, Inc.

KEY WORDS: mental retardation, autosomal dominant, short stature, dental caries

INTRODUCTION

The acrofacial dysostoses (AFD) are a heterogeneous group of disorders combining varying severities of mandibulofacial dysostosis (MFD) with pre and/or postaxial limb abnormalities. In 1993, Opitz et al. described a new AFD with mental retardation in a Sicilian mother and her four sons characterized by intrauterine growth retardation (IUGR), postnatal short stature, microcephaly, widow's peak, MFD without cleft palate, mild pre-and postaxial limb hypoplasia with brachydactyly, mild interdigital webbing, and cryptorchidism and hypospadias in males. We report on a mother and her daughter with this same phenotype confirming the Catania brachydactylous type of AFD and showing transmission consistent with autosomal dominant inheritance.

CLINICAL REPORTS

Patient 1

Our propositus was born at 1,440 g (<10th centile), after a pregnancy complicated only by premature delivery at 34 weeks gestation to a 24-year-old gravida 1 mother and a 25-year-old father. In the nursery, she never required respiratory support or oxygen, but was hospitalized for one month because of poor feeding and slow weight gain. At age 7 months, she was referred for genetic evaluation due to developmental delay and anomalies of the face and limbs. Cytologic analysis documented a normal GTG-banded karyotype, and a diagnosis of unknown AFD was made. She was re-evaluated at age 5-1/2 years after an uncomplicated interval medical history and functioned at a mild mental retardation level. Her height then was 105.7 cm (5th centile), weight 16.1 kg (5th centile), and a head circumference (OFC) of 48.5 cm (5th centile). She had a tall forehead, low anterior hairline, mild lateral facial hypoplasia, and abnormally modeled ears (Fig. 1a,b). The palate appeared high-arched. Her hands were 11.5 cm long (3rd centile) and showed brachydactyly with mild interdigital webbing, apparent proximal placement of the thumbs, and fifth finger brachyclinodactyly (Fig. 3a). Her feet were 16 cm long (3rd centile) with 2–3 toe syndactyly (Fig. 4a).

Patient 2

The mother of patient 1 weighed 2,000 g (10th centile) at birth, after a 36-week gestation to a 25-year-old mother and 33-year-old father. Details of the pregnancy, labor, and delivery are unavailable. She received

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Fig. 1. **(a)** Facial appearance of patient 1 (5½ years). **(b)** Lateral face of patient 1 (5½ years).

special education throughout childhood and currently functions at a mildly to moderately retarded level. At age 18 years, she had all of her upper teeth removed because of severe caries. At age 30 years, she was 152.8 cm tall, weighed 41.5 kg, and had a head circumference of 49 cm. Physical examination showed microcephaly, a tall forehead, low anterior hair line, a widow's peak, lateral facial hypoplasia, downward slant of the palpebral fissures, and mildly abnormal ears with small lobules (Fig. 2a,b). The palate appeared high-arched, and there were carious teeth in her lower jaw and an edentulous upper jaw. Her hands were small with a total length of 16 cm. They showed brachydactyly, mild interdigital webbing, apparent proximal placement of the thumbs, and hypoplasia of the second phalanx of the fifth fingers (Fig. 3b). Her feet were short with a length of 19.5 cm (Fig. 4b).

Metacarpophalangeal pattern profiles [Poznanski et al., 1972] were performed on these patients and compared to two of the patients reported by Opitz et al. [1993]. Although there was an overall shortness of all metacarpals and phalanges of between −2−−4 standard deviations, no distinct pattern of abnormality was discerned. Cephalometric analysis also showed no distinctive diagnostic pattern.

DISCUSSION

The acrofacial dysostoses are genetically heterogeneous. The sentinel disorders in this group of conditions are the Nager syndrome [Nager and de Reynier, 1948], combining MFD with predominant preaxial limb abnormalities, and the postaxial acrofacial dysostosis syndrome (PODS), sometimes referred to as the Miller [Miller et al., 1979] or Genée-Wiedemann syndrome [Genée, 1969; Wiedemann, 1973]. In addition, some half dozen other rare forms of acrofacial dysostoses have been described and were reviewed by Opitz et al. [1993].

Only two recognized acrofacial dysostoses can be considered multiple congenital anomaly-mental retardation (MCA/MR) syndromes: the AFD-MR syndrome of Kelly et al. [1977] and the Catania type of AFD [Opitz et al., 1993]. The Kelly type of AFD appears to be an autosomal recessive disorder characterized by in utero growth retardation, postnatal short stature, mental retardation, genital anomalies, and mild AFD, whereas the Catania type of AFD is most likely an autosomal dominant disorder.

The mother and daughter in this current family share the typical findings described by Opitz et al. [1993] in the Catania brachydactylous type of AFD. They are compared to those of the original family and summarized in Table I. Analysis of cephalometric and metacarpophalangeal profiles on this family showed no distinct patterns of abnormality useful for diagnosis. A manifestation noted, but not emphasized, in the original family is frequent dental caries. We conclude that the family reported here confirms and expands the phenotypic picture of the Catania brachydactylous type of AFD. Although we cannot exclude the possibility that this is a new type of AFD, we consider it highly unlikely. This family also supports autosomal dominant

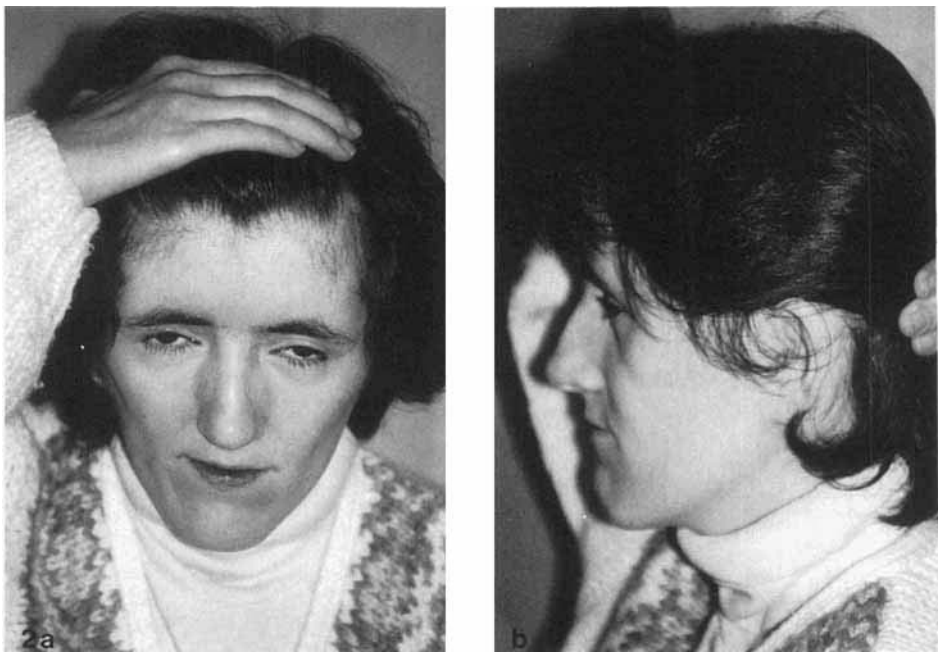

Fig. 2. **(a)** Facial appearance of patient 2 (30 years). **(b)** Lateral face of patient 2 (30 years).

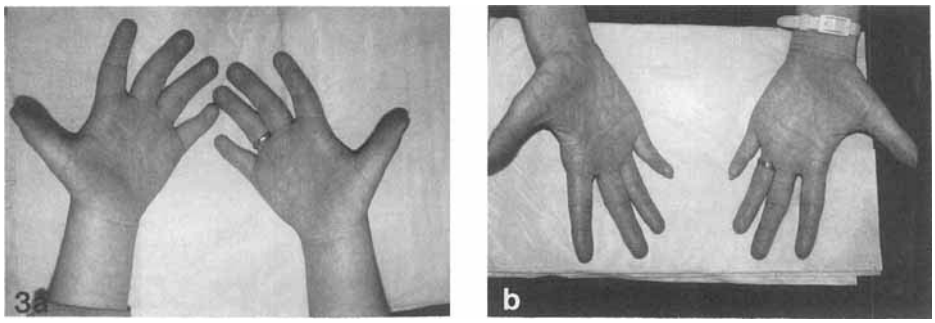

Fig. 3. **(a)** Hands of patient 1. **(b)** Hands of patient 2.

Fig. 4. **(a)** Foot of patient 1. **(b)** Foot of patient 2.

TABLE I. Clinical Features of Catania Type of Acrofacial Dysostosis

Finding	Opitz et al. [1993]	Current report	Total
Short stature	5/5	2/2	7/7
Mental retardation	5/5	2/2	7/7
Intrauterine growth retardation	2/4	2/2	4/6
Craniofacial			
Microcephaly	3/4	2/2	5/6
Malar hypoplasia (mild)	5/5	2/2	7/7
Sparse lateral eyebrows	2/2	1/2	3/4
High arched palate	3/3	2/2	5/5
Tall forehead	4/5	2/2	6/7
Widow's peak	5/5	1/2	6/7
Small or "dysplastic" ears	2/5	2/2	4/7
Micrognathia	4/4	0/2	4/6
Carious teeth	3/3	1/2	4/5
Limbs			
Brachydactyly	5/5	2/2	7/7
Short fifth finger	5/5	2/2	7/7
Fifth finger clinodactyly	1/3	1/2	2/5
Short thumb	4/4	1/2	5/6
Interdigital webbing (mild)	4/4	1/2	5/6
Other			
Cryptorchidism	3/4	na	3/4
Hypospadias	1/4	na	1/4
Inguinal hernia	2/5	0/2	2/7

inheritance for this condition, although male-to-male transmission has not been demonstrated.

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